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NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2	Apr 08	"Ask CAS" for self-help around the clock
NEWS	3	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS	4	Apr 09	ZDB will be removed from STN
NEWS	5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS	6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS	7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS	8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS	9	Jun 03	New e-mail delivery for search results now available
NEWS	10	Jun 10	MEDLINE Reload
NEWS	11	Jun 10	PCTFULL has been reloaded
NEWS	12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS	13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
NEWS	14	Jul 29	Enhanced polymer searching in REGISTRY
NEWS	15	Jul 30	NETFIRST to be removed from STN
NEWS	16	Aug 08	CANCERLIT reload
NEWS	17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
NEWS	18	Aug 08	NTIS has been reloaded and enhanced
NEWS	19	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS	20	Aug 19	IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS	21	Aug 19	The MEDLINE file segment of TOXCENTER has been reloaded
NEWS	22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS	23	Sep 03	JAPIO has been reloaded and enhanced
NEWS	24	Sep 16	Experimental properties added to the REGISTRY file
NEWS	25	Sep 16	CA Section Thesaurus available in CAPLUS and CA
NEWS	26	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
NEWS	27	Oct 21	EVENTLINE has been reloaded
NEWS	28	Oct 24	BEILSTEIN adds new search fields
NEWS	29	Oct 24	Nutraceuticals International (NUTRACEUT) now available on STN
NEWS	30	Oct 25	MEDLINE SDI run of October 8, 2002
NEWS	31	Nov 18	DKILIT has been renamed APOLLIT
NEWS	32	Nov 25	More calculated properties added to REGISTRY
NEWS	33	Dec 02	TIBKAT will be removed from STN
NEWS	34	Dec 04	CSA files on STN
NEWS	35	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS	36	Dec 17	TOXCENTER enhanced with additional content
NEWS	37	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS	38	Dec 30	ISMEC no longer available
NEWS	39	Jan 13	Indexing added to some pre-1967 records in CA/CAPLUS
NEWS	40	Jan 21	NUTRACEUT offering one free connect hour in February 2003
NEWS	41	Jan 21	PHARMAML offering one free connect hour in February 2003
NEWS	42	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC

NEWS EXPRESS January 6 CURRENT WINDOWS VERSION IS V6.01a,
CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),

```
                AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
 NEWS HOURS     STN Operating Hours Plus Help Desk Availability
 NEWS INTER     General Internet Information
 NEWS LOGIN     Welcome Banner and News Items
 NEWS PHONE     Direct Dial and Telecommunication Network Access to STN
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FILE 'HOME' ENTERED AT 14:43:21 ON 06 FEB 2003

=> fil reg
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'REGISTRY' ENTERED AT 14:43:40 ON 06 FEB 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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STRUCTURE FILE UPDATES:    5 FEB 2003  HIGHEST RN 486392-61-4
DICTIONARY FILE UPDATES:   5 FEB 2003  HIGHEST RN 486392-61-4

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>
Uploading 09815362b.str

L1      STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1              STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *
```

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 14:43:58 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   2453 TO ITERATE

 40.8% PROCESSED   1000 ITERATIONS   50 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS: 46090 TO   52030
PROJECTED ANSWERS: 5937 TO   8191

L2   50 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 14:44:01 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 49870 TO ITERATE

100.0% PROCESSED   49870 ITERATIONS   6932 ANSWERS
SEARCH TIME: 00.00.03

L3   6932 SEA SSS FUL L1

=>
Uploading 09815362b.str

L4   STRUCTURE UPLOADED

=> d
L4 HAS NO ANSWERS
L4   STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l4
SAMPLE SEARCH INITIATED 14:46:10 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   6223 TO ITERATE

 16.1% PROCESSED   1000 ITERATIONS   0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS: 119734 TO   129186
PROJECTED ANSWERS: 0 TO   0

L5   0 SEA SSS SAM L4

=> s l4 full
FULL SEARCH INITIATED 14:46:15 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 124728 TO ITERATE

[redacted]

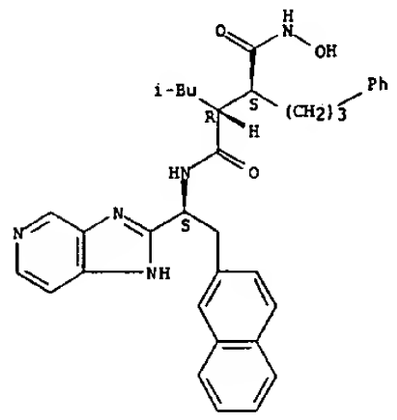
100.0% PROCESSED 124728 ITERATIONS 26 ANSWERS
SEARCH TIME: 00.00.02

L6 26 SEA SSS FUL L4

=> d scan

L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Butanediamide, N4-hydroxy-N1-[1-(1H-imidazo[4,5-c]pyridin-2-yl)-2-(2-naphthalenyl)ethyl]-2-(2-methylpropyl)-3-(3-phenylpropyl)-, [2R-[1(S*),2R*,3S*]]- (9CI)
MF C35 H39 N5 O3

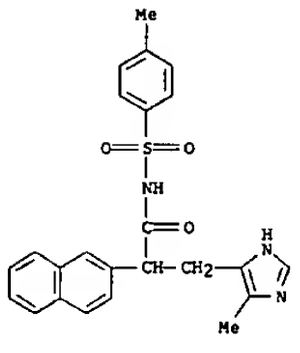
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):25

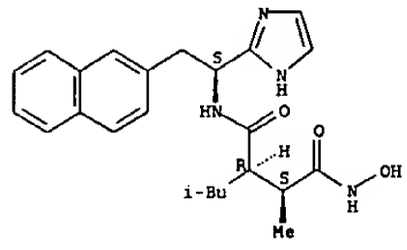
L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 1H-Imidazole-4-propanamide, 5-methyl-N-[(4-methylphenyl)sulfonyl]-.alpha.-2-naphthalenyl- (9CI)
MF C24 H23 N3 O3 S



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Butanediamide, N1-hydroxy-N4-[1-(1H-imidazol-2-yl)-2-(2-naphthalenyl)ethyl]-2-methyl-3-(2-methylpropyl)-, [2S-[2R*,3S*,4(R*)]]- (9CI)
MF C24 H30 N4 O3

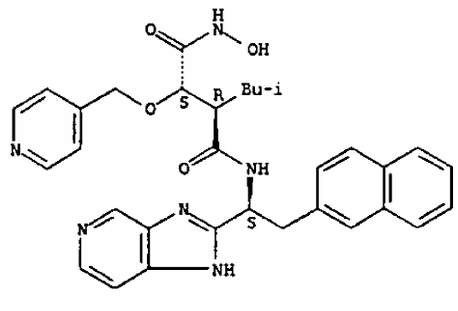
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Butanediamide, N4-hydroxy-N1-[1-(1H-imidazo[4,5-c]pyridin-2-yl)-2-(2-naphthalenyl)ethyl]-2-(2-methylpropyl)-3-(4-pyridinylmethoxy)-, [2R-[1(S*),2R*,3S*]]- (9CI)
MF C32 H34 N6 O4

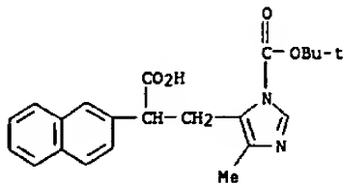
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

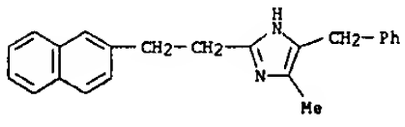
[redacted]

L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 1H-Imidazole-5-propanoic acid, 1-[(1,1-dimethylethoxy)carbonyl]-4-methyl-.alpha.-2-naphthalenyl- (9CI)
MF C22 H24 N2 O4



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

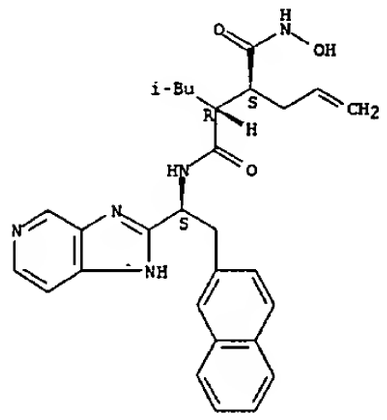
L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 1H-Imidazole, 4-methyl-2-[2-(2-naphthalenyl)ethyl]-5-(phenylmethyl)- (9CI)
MF C23 H22 N2



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Butanediamide, N4-hydroxy-N1-[1-(1H-imidazo[4,5-c]pyridin-2-yl)-2-(2-naphthalenyl)ethyl]-2-(2-methylpropyl)-3-(2-propenyl)-, [2R-[1(S*),2R*,3S*]]- (9CI)
MF C29 H33 N5 O3

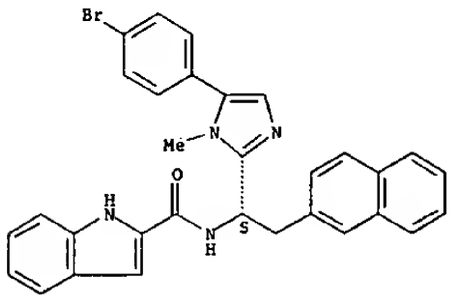
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 1H-Indole-2-carboxamide, N-[(1S)-1-[5-(4-bromophenyl)-1-methyl-1H-imidazol-2-yl]-2-(2-naphthalenyl)ethyl]- (9CI)
MF C31 H25 Br N4 O

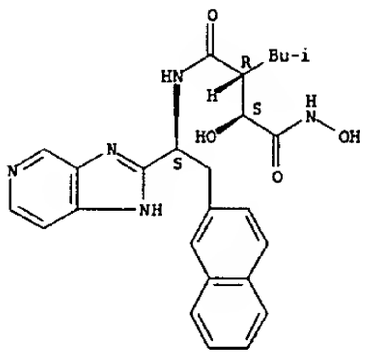
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

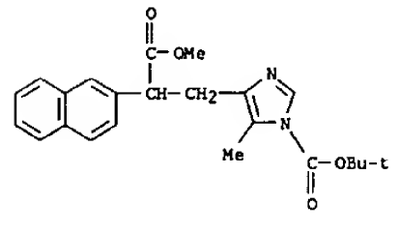
L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Butanediamide, N1,2-dihydroxy-N4-[1-(1H-imidazo[4,5-c]pyridin-2-yl)-2-(2-naphthalenyl)ethyl]-3-(2-methylpropyl)-, [2S-[2R*,3S*,4(R*)]]- (9CI)
MF C26 H29 N5 O4

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

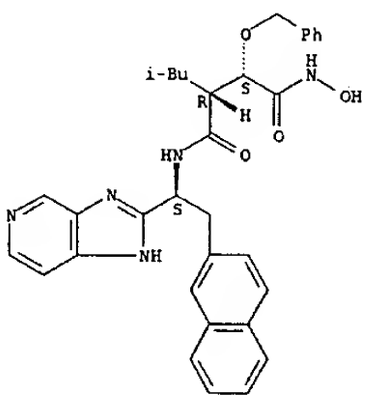
L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 1H-Imidazole-4-propanoic acid, 1-[(1,1-dimethylethoxy)carbonyl]-5-methyl-.alpha.-2-naphthalenyl-, methyl ester (9CI)
MF C23 H26 N2 O4



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

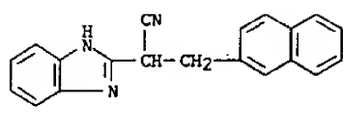
L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Butanediamide, N4-hydroxy-N1-[1-(1H-imidazo[4,5-c]pyridin-2-yl)-2-(2-naphthalenyl)ethyl]-2-(2-methylpropyl)-3-(phenylmethoxy)-, [2R-[1(S*),2R*,3S*]]- (9CI)
MF C33 H35 N5 O4

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

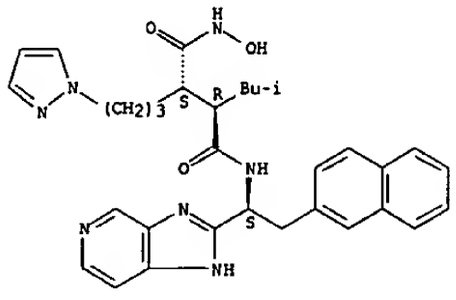
L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 1H-Benzimidazole-2-acetonitrile, .alpha.-(2-naphthalenylmethyl)- (9CI)
MF C20 H15 N3



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

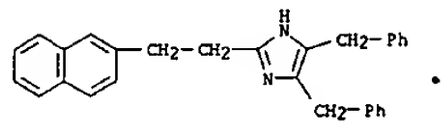
L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Butanediamide, N4-hydroxy-N1-[1-(1H-imidazo[4,5-c]pyridin-2-yl)-2-(2-naphthalenyl)ethyl]-2-(2-methylpropyl)-3-[3-(1H-pyrazol-1-yl)propyl]-, [2R-[1(S*),2R*,3S*]]- (9CI)
MF C32 H37 N7 O3

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

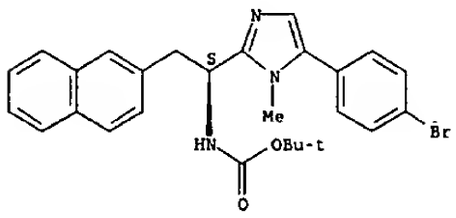
L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 1H-Imidazole, 2-[2-(2-naphthalenyl)ethyl]-4,5-bis(phenylmethyl)- (9CI)
MF C29 H26 N2



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Carbamic acid, [(1S)-1-[5-(4-bromophenyl)-1-methyl-1H-imidazol-2-yl]-2-(2-naphthalenyl)ethyl]-, 1,1-dimethylethyl ester (9CI)
MF C27 H28 Br N3 O2

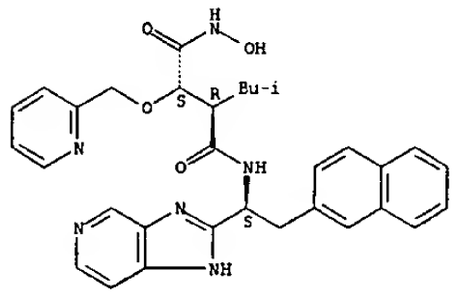
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

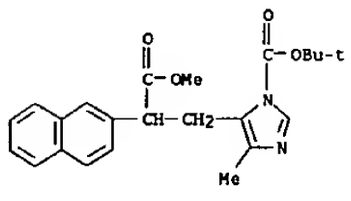
L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Butanediamide, N4-hydroxy-N1-[1-(1H-imidazo[4,5-c]pyridin-2-yl)-2-(2-naphthalenyl)ethyl]-2-(2-methylpropyl)-3-(2-pyridinylmethoxy)-, [2R-[1(S*),2R*,3S*]]- (9CI)
MF C32 H34 N6 O4

Absolute stereochemistry.



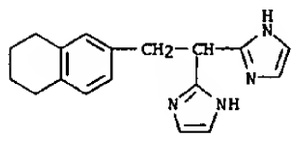
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 1H-Imidazole-5-propanoic acid, 1-[(1,1-dimethylethoxy)carbonyl]-4-methyl-.alpha.-2-naphthalenyl-, methyl ester (9CI)
MF C23 H26 N2 O4



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

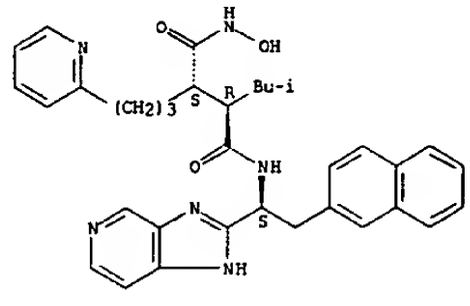
L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 1H-Imidazole, 2,2'-[2-(5,6,7,8-tetrahydro-2-naphthalenyl)ethylidene]bis- (9CI)
MF C18 H20 N4



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Butanediamide, N4-hydroxy-N1-[1-(1H-imidazo[4,5-c]pyridin-2-yl)-2-(2-naphthalenyl)ethyl]-2-(2-methylpropyl)-3-[3-(2-pyridinyl)propyl]-, [2R-[1(S*),2R*,3S*]]- (9CI)
MF C34 H38 N6 O3

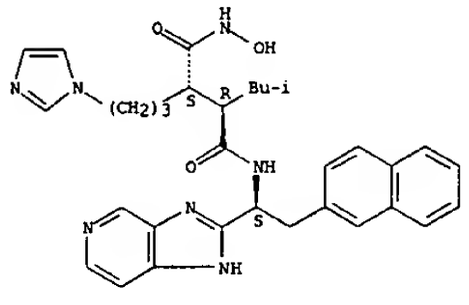
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Butanediamide, N1-hydroxy-N4-[1-(1H-imidazo[4,5-c]pyridin-2-yl)-2-(2-naphthalenyl)ethyl]-2-[3-(1H-imidazol-1-yl)propyl]-3-(2-methylpropyl)-, [2S-[2R*,3S*,4(R*)]]- (9CI)
MF C32 H37 N7 O3

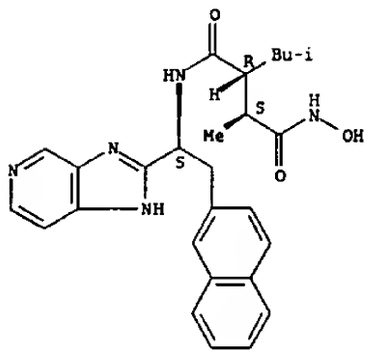
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Butanediamide, N1-hydroxy-N4-[1-(1H-imidazo[4,5-c]pyridin-2-yl)-2-(2-naphthalenyl)ethyl]-2-methyl-3-(2-methylpropyl)-, [2S-[2R*,3S*,4(R*)]]- (9CI)
MF C27 H31 N5 O3

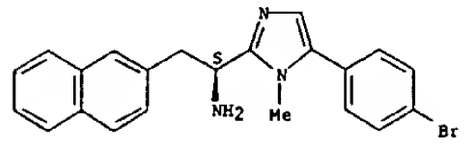
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 1H-Imidazole-2-methanamine, 5-(4-bromophenyl)-1-methyl-.alpha.-(2-naphthalenylmethyl)-, (.alpha.S)- (9CI)
MF C22 H20 Br N3

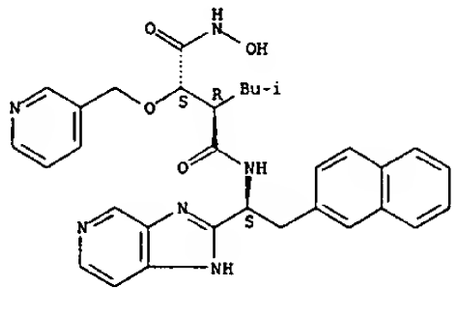
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

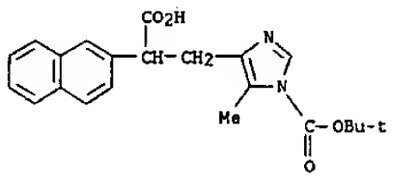
L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Butanediamide, N4-hydroxy-N1-[1-(1H-imidazo[4,5-c]pyridin-2-yl)-2-(2-naphthalenyl)ethyl]-2-(2-methylpropyl)-3-(3-pyridinylmethoxy)-, [2R-[1(S*),2R*,3S*]]- (9CI)
MF C32 H34 N6 O4

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

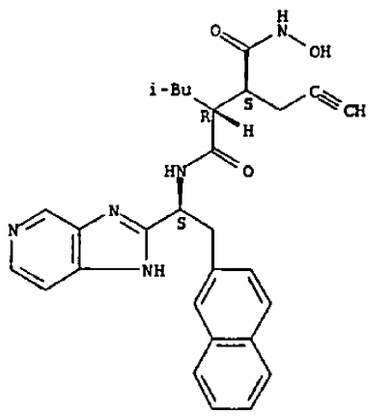
L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 1H-Imidazole-4-propanoic acid, 1-[(1,1-dimethylethoxy)carbonyl]-5-methyl-.alpha.-2-naphthalenyl- (9CI)
MF C22 H24 N2 O4



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

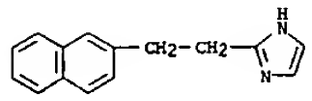
L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Butanediamide, N4-hydroxy-N1-[1-(1H-imidazo[4,5-c]pyridin-2-yl)-2-(2-naphthalenyl)ethyl]-2-(2-methylpropyl)-3-(2-propynyl)-, [2R-[1(S*),2R*,3S*]]- (9CI)
MF C29 H31 N5 O3

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 26 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN 1H-Imidazole, 2-[2-(2-naphthalenyl)ethyl]- (9CI)
MF C15 H14 N2



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

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Uploading 09815362b.str

L7      STRUCTURE UPLOADED

=> d
L7 HAS NO ANSWERS
L7                STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.


=> s l7
SAMPLE SEARCH INITIATED 14:48:42 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -   6223 TO ITERATE

 16.1% PROCESSED    1000 ITERATIONS                                 7 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       119734 TO   129186
PROJECTED ANSWERS:             475 TO     1267

L8             7 SEA SSS SAM L7

=> s l7 full
FULL SEARCH INITIATED 14:48:45 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 124728 TO ITERATE

100.0% PROCESSED  124728 ITERATIONS                           464 ANSWERS
SEARCH TIME: 00.00.02

L9           464 SEA SSS FUL L7

=> fil caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                              446.85     447.06

FILE 'CAPLUS' ENTERED AT 14:48:51 ON 06 FEB 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)
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[redacted]

FILE COVERS 1907 - 6 Feb 2003 VOL 138 ISS 6
FILE LAST UPDATED: 5 Feb 2003 (20030205/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

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=> s l9
L10          67 L9

=> s l10 and adrenergic
          68996 ADRENERGIC
            255 ADRENERGICS
          69040 ADRENERGIC
                  (ADRENERGIC OR ADRENERGICS)
L11           8 L10 AND ADRENERGIC

=> d ibib abs hitstr 1-8
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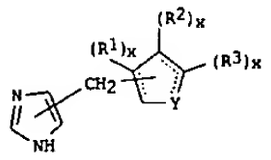
[redacted]

L11 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:754359 CAPLUS
DOCUMENT NUMBER: 137:263032
TITLE: Preparation of imidazoles as selective agonists at .alpha.2B or .alpha.2B/.alpha.2C adrenergic receptors
INVENTOR(S): Chow, Ken; Gil, Daniel W.; Burke, James A.; Harcourt, Dale A.; Garst, Michael E.; Wheeler, Larry A.; Munk, Stephen A.; Gomez, Dario G.
PATENT ASSIGNEE(S): Allergan, Inc., USA
SOURCE: PCT Int. Appl., 141 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002076950	A2	20021003	WO 2002-US8222	20020313
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003023098	A1	20030130	US 2001-815362	20010321

PRIORITY APPLN. INFO.: US 2001-815362 A 20010321
US 1997-985347 B2 19971204
US 1998-205597 B2 19981204
US 1999-329752 B2 19990610

OTHER SOURCE(S): MARPAT 137:263032
GI

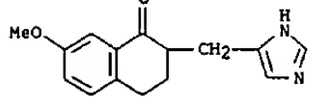


I

AB Compds. (shown as I), which are selective agonists at .alpha.2B or .alpha.2B/.alpha.2C adrenergic receptors and useful for the treatment of conditions including pain, particularly chronic pain, glaucoma or elevated intraocular pressure with reduced cardiovascular or sedative side effects, are claimed. Also included are methods of making and using such compds. In I, each x is independently 1 or 2; each R1 is independently H; halogen; C1-4 alkyl; C1-4 alkenyl; C1-4 alkynyl; -COR4 where R4 is H, C1-4 alkyl or C1-4 alkoxy; C3-6 cycloalkyl; aryl; heteroaryl; cyano; nitro; trihalomethyl; oxo; or -(CH2)n-X-(CH2)m-(R5)o where X is O, S or N, n is 0-3, m is 0-3, o is 0-1, and R5 is Me or H1-2. Each R2 and each R3 are independently H; halogen; C1-4 alkyl; C1-4 alkenyl; C1-4 alkynyl; -COR4 where R4 is H; C1-4 alkyl or C1-4 alkoxy; C3-6 cycloalkyl; aryl; heteroaryl; cyano; nitro; trihalomethyl; oxo; or -(CH2)n-X-(CH2)m-(R5)o where X is O, S or N, n is 0-3, m is 0-3, o is 0-1, and R5 is Me or H1-2; or an R2 and an R3 together condense to form a satd., partly satd., or unsatd. ring structure having the formula -[C(R6)p]q-Xs-[C(R6)p]r-Xt-[C(R6)p]u where each R6 is independently H; halogen; C1-4 alkyl; C1-4 alkenyl; C1-4 alkynyl; -COR4 where R4 is H, C1-4 alkyl or C1-4 alkoxy; C3-6 cycloalkyl; aryl; heteroaryl; cyano; nitro; trihalomethyl and oxo where each p is independently 1 or 2, q is 0-5, r is 0-5, u is 0-5. Each X is independently O, S, or N and s is 0 or 1; provided that q + r + u + s + t < 6. Y is O; S; N; -[C(R7)z]s-, where each R7 is independently as previously defined for R1, each z is independently 1-2, and s is 1-3; -CH: ; -CH:CH-; or Y1CH2, where Y1 is O, N, or S; and the dotted lines in I are optional double bonds, with the proviso that if the ring including Y is a cyclohexane ring or a heterocyclic 5 member ring said ring is not fully unsatd., and that if Y is O, N or S, the ring including Y contains at least one said double bond. Intrinsic activities towards .alpha.2A, .alpha.2B, .alpha.2C adrenergic receptors of .apprx.100 of the claimed compds. relative to brimonidine/oxymetazoline are tabulated. Although the methods of prepn. are not claimed, .apprx.100 example prepns. are included.

IT 157058-47-4P, 1(2H)-Naphthalenone, 3,4-dihydro-2-(1H-imidazol-4-ylmethyl)-7-methoxy-
RL: BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of imidazoles as selective agonists at .alpha.2b or .alpha.2b/.alpha.2c adrenergic receptors)

RN 157058-47-4 CAPLUS
CN 1(2H)-Naphthalenone, 3,4-dihydro-2-(1H-imidazol-4-ylmethyl)-7-methoxy- (9CI) (CA INDEX NAME)



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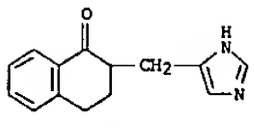
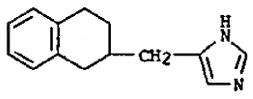
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of imidazoles as selective agonists at .alpha.2b or .alpha.2b/.alpha.2c adrenergic receptors)

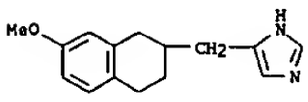
RN 157058-44-1 CAPLUS
CN 1(2H)-Naphthalenone, 3,4-dihydro-2-(1H-imidazol-4-ylmethyl)- (9CI) (CA INDEX NAME)



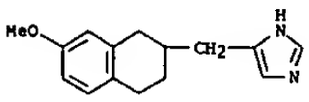
RN 157058-52-1 CAPLUS
CN 1H-Imidazole, 4-[(1,2,3,4-tetrahydro-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)



RN 157058-55-4 CAPLUS
CN 1H-Imidazole, 4-[(1,2,3,4-tetrahydro-7-methoxy-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)



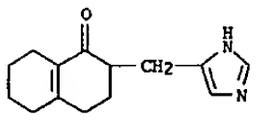
RN 226570-89-4 CAPLUS
CN 1H-Imidazole, 4-[(1,2,3,4-tetrahydro-7-methoxy-2-naphthalenyl)methyl]-, monohydrochloride (9CI) (CA INDEX NAME)



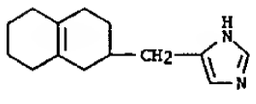
● HCl

L11 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 226571-02-4 CAPLUS
CN 1(2H)-Naphthalenone, 3,4,5,6,7,8-hexahydro-2-(1H-imidazol-4-ylmethyl)- (9CI) (CA INDEX NAME)

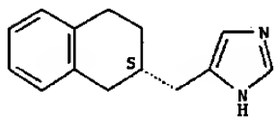


RN 226571-05-7 CAPLUS
CN 1H-Imidazole, 4-[(1,2,3,4,5,6,7,8-octahydro-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)



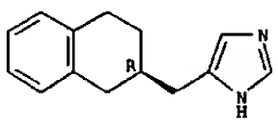
RN 226571-13-7 CAPLUS
CN 1H-Imidazole, 4-[[(2S)-1,2,3,4-tetrahydro-2-naphthalenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



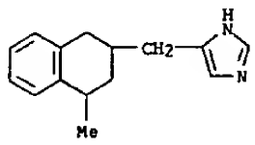
RN 226571-14-8 CAPLUS
CN 1H-Imidazole, 4-[[(2R)-1,2,3,4-tetrahydro-2-naphthalenyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

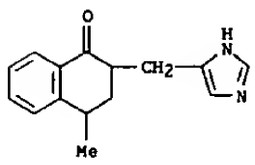


RN 226571-25-1 CAPLUS
CN 1H-Imidazole, 4-[(1,2,3,4-tetrahydro-4-methyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)

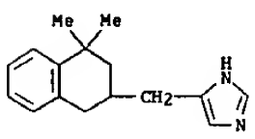
L11 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2003 ACS (Continued)



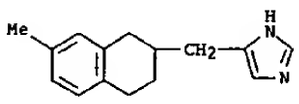
RN 226571-26-2 CAPLUS
CN 1(2H)-Naphthalenone, 3,4-dihydro-2-(1H-imidazol-4-ylmethyl)-4-methyl-(9CI) (CA INDEX NAME)



RN 226571-35-3 CAPLUS
CN 1H-Imidazole, 4-[(1,2,3,4-tetrahydro-4,4-dimethyl-2-naphthalenyl)methyl]-(9CI) (CA INDEX NAME)



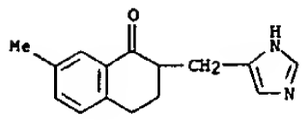
RN 226571-36-4 CAPLUS
CN 1H-Imidazole, 4-[(1,2,3,4-tetrahydro-7-methyl-2-naphthalenyl)methyl]-, monohydrochloride (9CI) (CA INDEX NAME)



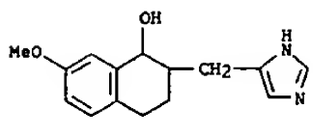
● HCl

RN 226571-37-5 CAPLUS
CN 1(2H)-Naphthalenone, 3,4-dihydro-2-(1H-imidazol-4-ylmethyl)-7-methyl-(9CI) (CA INDEX NAME)

L11 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2003 ACS (Continued)



IT 226571-57-9P, 1-Naphthalenol, 1,2,3,4-tetrahydro-2-(1H-imidazol-4-ylmethyl)-7-methoxy-
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of imidazoles as selective agonists at .alpha.2b or .alpha.2b/.alpha.2c adrenergic receptors)
RN 226571-57-9 CAPLUS
CN 1-Naphthalenol, 1,2,3,4-tetrahydro-2-(1H-imidazol-4-ylmethyl)-7-methoxy-(9CI) (CA INDEX NAME)

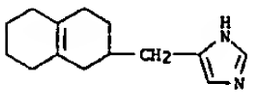


L11 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:353314 CAPLUS
DOCUMENT NUMBER: 136:365878
TITLE: Methods and compositions for treatment of ocular neovascularization and neural injury
INVENTOR(S): Burke, James A.; Lin, Ton; Wheeler, Larry A.; De Vries, Gerald W.
PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

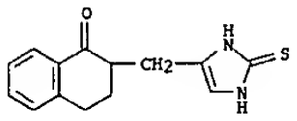
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002036162	A2	20020510	WO 2001-US46014	20011101
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002030567	A5	20020515	AU 2002-30567	20011101
US 2002094998	A1	20020718	US 2001-998718	20011101
PRIORITY APPLN. INFO.:			US 2000-244850P P	20001101
			WO 2001-US46014 W	20011101

AB Methods and compns. for the treatment of ocular neovascularization (CNV) and macular degeneration are disclosed. The invention includes combining laser treatment with administration of a neuroprotectant. Seven pigmented rabbits were dosed with either 0.5 mL 0.2% brimonidine or saline administered in 1 eye of each rabbit. One hour later, the animals were treated with a 10-min i.v. infusion of 0.2 mg/kg verteporfin, then the same eye was irradiated 10 min later in the lower fundus with a 689-nm diode laser at 50 J/cm2, 600 mW/cm2 and a spot size of 1.5 mm. Brimonidine reduced the increase in retinal thickness (subretinal cyst + retina) in the lesion produced by PDT.
IT 226571-05-7, AGN 795 423773-40-4, AGN 960
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for treatment of ocular neovascularization and neural injury)
RN 226571-05-7 CAPLUS
CN 1H-Imidazole, 4-[(1,2,3,4,5,6,7,8-octahydro-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)



RN 423773-40-4 CAPLUS
CN 1(2H)-Naphthalenone, 2-[(2,3-dihydro-2-thioxo-1H-imidazol-4-yl)methyl]-3,4-dihydro- (9CI) (CA INDEX NAME)

L11 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2003 ACS (Continued)



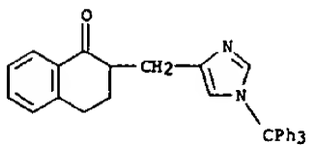
[redacted]

L11 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:85068 CAPLUS
DOCUMENT NUMBER: 134:260881
TITLE: Potential Antidepressants Displayed Combined .alpha.2-Adrenoceptor Antagonist and Monoamine Uptake Inhibitor Properties
AUTHOR(S): Cordi, Alex A.; Berque-Bestel, Isabelle; Persigand, Thierry; Lacoste, Jean-Michel; Newman-Tancredi, Adrian; Audinot, Valerie; Millan, Mark J.
CORPORATE SOURCE: Institut de Recherches Servier, Suresnes, F-92150, Fr.
SOURCE: Journal of Medicinal Chemistry (2001), 44(5), 787-805
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Classical antidepressants are thought to act by raising monoamine (serotonin and noradrenaline) levels in the brain. This action is generally accomplished either by inhibition of monoamine metab. (MAO inhibitors) or by blockade of monoamine uptake (tricyclic antidepressants and selective serotonin or noradrenaline reuptake inhibitors). However, all such agents suffer from a time lag (3-6 wk) before robust clin. efficacy can be demonstrated. This delay may reflect inhibitory actions of noradrenaline at presynaptic .alpha.2A-adrenergic auto- or heteroreceptors which gradually down-regulate upon prolonged exposure. Blockade of presynaptic .alpha.2A-adrenoceptors by an antagonist endowed with monoamine uptake inhibition properties could lead to new antidepressants with greater efficacy and a shorter time lag. In the literature, only two mols. have been described with such a pharmacol. profile. Of these, napamezole was chosen as a point of departure for the design of 4(5)-[(3,4-dihydro-2-naphthalenyl)methyl]-4,5-dihydroimidazole, which displayed the desired profile: .alpha.2A-adrenoceptor antagonist properties and serotonin/noradrenaline uptake inhibition. From this original mol., a series of derivs. was designed and synthesized, encompassing substituted as well as rigid analogs. Structure-activity relationships permitted the selection of (4(5)-[(5-fluoroindan-2-yl)methyl]-4,5-dihydroimidazole) as a development candidate.

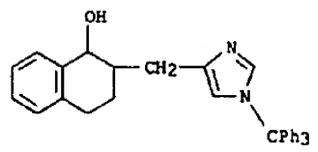
IT **331992-77-9P 331992-78-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and structure-activity relations of potential antidepressants displaying combined .alpha.2-adrenoceptor antagonist and monoamine uptake inhibitor activities)

RN 331992-77-9 CAPLUS
CN 1(2H)-Naphthalenone, 3,4-dihydro-2-[[1-(triphenylmethyl)-1H-imidazol-4-yl]methyl]- (9CI) (CA INDEX NAME)



RN 331992-78-0 CAPLUS

L11 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2003 ACS (Continued)
CN 1-Naphthalenol, 1,2,3,4-tetrahydro-2-{[1-(triphenylmethyl)-1H-imidazol-4-yl]methyl]- (9CI) (CA INDEX NAME)



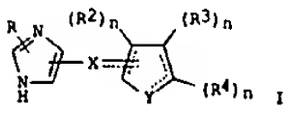
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:12424 CAPLUS
DOCUMENT NUMBER: 134:86245
TITLE: Preparation of imidazoles as selective agonists at .alpha.2b or .alpha.2b/.alpha.2c adrenergic receptors.
INVENTOR(S): Chow, Ken; Gil, Daniel W.; Burke, James A.; Harcourt, Dale A.; Garst, Michael E.; Wheeler, Larry A.; Munk, Stephen A.
PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001000586	A1	20010104	WO 2000-US15795	20000608
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1104407	A1	20010606	EP 2000-939699	20000608
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2002156076	A1	20021024	US 2001-948001	20010906

PRIORITY APPLN. INFO.: US 1999-329752 A 19990610
US 1997-985347 B2 19971204
US 1998-205597 B2 19981204
WO 2000-US15795 W 20000608
US 2000-679919 A1 20001005

OTHER SOURCE(S): MARPAT 134:86245
GI



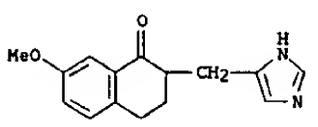
I

AB Title compds. [I; dotted lines = optional double bonds; R = H, alkyl; X = S, CHR1; R1 = H, alkyl, null; Y = O, N, S, [C(R1)n]y, CH:CH, YlCH2; y = 1-3; n = 1, 2; R2 = H, alkyl, halo, OH, alkoxy, alkenyl, acyl, alkynyl, etc.; R3, R4 = H, alkyl, halo, alkenyl, acyl, alkynyl, etc.; R3R4 = atoms to form (unsatd.) (heterocyclic) ring], were prepd. Thus, 1-(dimethylsulfamoyl)imidazole in THF at -78.degree. was treated with BuLi and tert-butyldimethylsilyl chloride followed by warming to room temp., stirring overnight, cooled to -20.degree., and treatment with BuLi and 3-thiophenecarboxaldehyde followed by warming to room temp. and stirring

L11 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS (Continued)
overnight to give 2-(tert-butyldimethylsilyl)-5-(hydroxythiophen-2-ylmethyl)imidazole-1-sulfonic acid dimethylamide. This was treated sequentially with Bu4NF, Et3SiH/CF3CO2H/CH2Cl2, and aq. HCl to give 4(5)-thiophen-3-ylmethyl-1H-imidazole. Tested I as eyedrops at 0.03-1% reduced intraocular pressure in cynomolgus monkeys by 12.4-33% and showed no sedative activity.

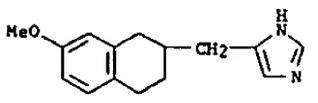
IT **157058-47-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of imidazoles as selective agonists at .alpha.2b or .alpha.2b/.alpha.2c adrenergic receptors)

RN 157058-47-4 CAPLUS
CN 1(2H)-Naphthalenone, 3,4-dihydro-2-(1H-imidazol-4-ylmethyl)-7-methoxy- (9CI) (CA INDEX NAME)

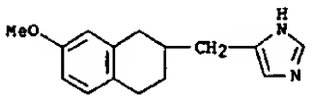


IT **157058-55-4P 226570-89-4P 226571-02-4P 226571-05-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of imidazoles as selective agonists at .alpha.2b or .alpha.2b/.alpha.2c adrenergic receptors)

RN 157058-55-4 CAPLUS
CN 1H-Imidazole, 4-[(1,2,3,4-tetrahydro-7-methoxy-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)

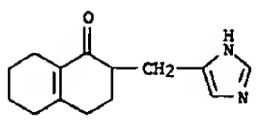


RN 226570-89-4 CAPLUS
CN 1H-Imidazole, 4-[(1,2,3,4-tetrahydro-7-methoxy-2-naphthalenyl)methyl]-, monohydrochloride (9CI) (CA INDEX NAME)

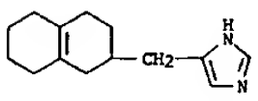


● HCl

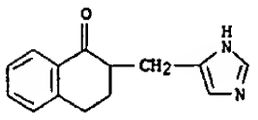
L11 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS (Continued)
RN 226571-02-4 CAPLUS
CN 1(2H)-Naphthalenone, 3,4,5,6,7,8-hexahydro-2-(1H-imidazol-4-ylmethyl)- (9CI) (CA INDEX NAME)



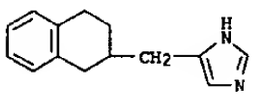
RN 226571-05-7 CAPLUS
CN 1H-Imidazole, 4-[(1,2,3,4,5,6,7,8-octahydro-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)



IT **157058-44-1 157058-52-1 226571-13-7 226571-14-8 226571-25-1 226571-26-2 226571-35-3 226571-36-4 226571-37-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of imidazoles as selective agonists at .alpha.2b or .alpha.2b/.alpha.2c **adrenergic** receptors)
RN 157058-44-1 CAPLUS
CN 1(2H)-Naphthalenone, 3,4-dihydro-2-(1H-imidazol-4-ylmethyl)- (9CI) (CA INDEX NAME)

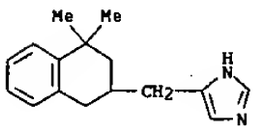


RN 157058-52-1 CAPLUS
CN 1H-Imidazole, 4-[(1,2,3,4-tetrahydro-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)

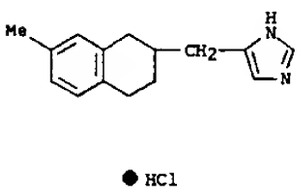


RN 226571-13-7 CAPLUS
CN 1H-Imidazole, 4-[[(2S)-1,2,3,4-tetrahydro-2-naphthalenyl]methyl]- (9CI)

L11 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS (Continued)
(9CI) (CA INDEX NAME)



RN 226571-36-4 CAPLUS
CN 1H-Imidazole, 4-[(1,2,3,4-tetrahydro-7-methyl-2-naphthalenyl)methyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 226571-37-5 CAPLUS
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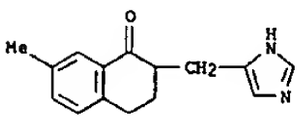
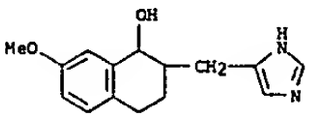


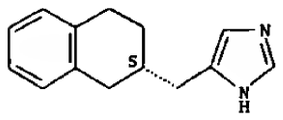
IT **226571-57-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of imidazoles as selective agonists at .alpha.2b or .alpha.2b/.alpha.2c **adrenergic** receptors)
RN 226571-57-9 CAPLUS
CN 1-Naphthalenol, 1,2,3,4-tetrahydro-2-(1H-imidazol-4-ylmethyl)-7-methoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

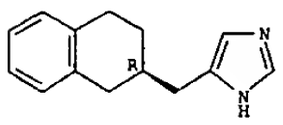
L11 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2003 ACS (Continued)
(CA INDEX NAME)

Absolute stereochemistry.

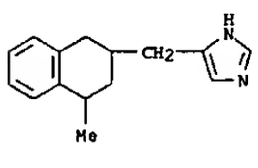


RN 226571-14-8 CAPLUS
CN 1H-Imidazole, 4-[[(2R)-1,2,3,4-tetrahydro-2-naphthalenyl]methyl]- (9CI) (CA INDEX NAME)

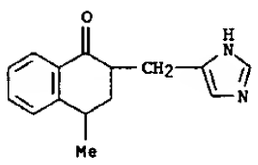
Absolute stereochemistry.



RN 226571-25-1 CAPLUS
CN 1H-Imidazole, 4-[(1,2,3,4-tetrahydro-4-methyl-2-naphthalenyl)methyl]- (9CI) (CA INDEX NAME)

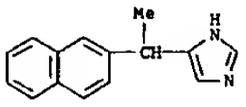


RN 226571-26-2 CAPLUS
CN 1(2H)-Naphthalenone, 3,4-dihydro-2-(1H-imidazol-4-ylmethyl)-4-methyl- (9CI) (CA INDEX NAME)



RN 226571-35-3 CAPLUS
CN 1H-Imidazole, 4-[(1,2,3,4-tetrahydro-4,4-dimethyl-2-naphthalenyl)methyl]-

L11 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:612212 CAPLUS
DOCUMENT NUMBER: 123:198691
TITLE: Medetomidine analogs as .alpha.-**adrenergic** agonists
AUTHOR(S): Amemiya, Yoshiya; Hus, Fulian; Shams, Gamal; Feller, Dennis R.; Venkataraman, B. V.; Patil, Popat N.; Miller, Duane D.
CORPORATE SOURCE: College Pharmacy, Ohio State University, Columbus, OH, 43210, USA
SOURCE: Egyptian Journal of Pharmaceutical Sciences (1994), 35(1-6), 403-10
CODEN: EJPSBZ; ISSN: 0301-5068
PUBLISHER: National Information and Documentation Centre
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 123:198691
AB Recently, it has been reported that medetomidine is a new 4-substituted imidazole analog possessing selective and potent .alpha.2-**adrenergic** properties. It has been shown that it reduces blood pressure, heart rate and saliva secretion. At the present time is sedative and hypotensive effects seem to be manifest in the same dose range. We have initiated a program to see if it is possible to sep. these activities with analogs of medetomidine. The initial studies have been directed at procedures for the conversion of the imidazolines, a common structure of .alpha.-**adrenergic** drugs, to the corresponding imidazoles. It was found that 2-substituted and 2,4-disubstituted imidazolines can easily be converted into imidazoles using 10% Pd/C in refluxing toluene, while in some instances there are some difficulties with the conversion of 4-substituted imidazolines to the imidazoles. The synthesis of 1- or 2-(2-or 4-imidazolylmethyl)naphthalene analogs of medetomidine are also described.
IT **137967-88-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of 4-substituted imidazoles)
RN 137967-88-5 CAPLUS
CN 1H-Imidazole, 4-[1-(2-naphthalenyl)ethyl]- (9CI) (CA INDEX NAME)



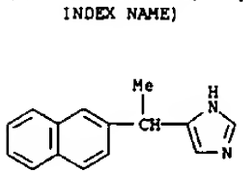
[redacted]

L11 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:612188 CAPLUS
DOCUMENT NUMBER: 123:111932
TITLE: Synthesis and .alpha.-adrenergic activities of 2- and 4-substituted imidazoline and imidazole analogs of .alpha.- and .beta.-naphthalene
AUTHOR(S): Amemiya, Yoshiya; Venkataraman, Burrah V.; Patil, Popat N.; Shams, Gamal; Romstedt, Karl
CORPORATE SOURCE: College Pharmacy, Ohio State University, Columbus, OH, 43210, USA
SOURCE: Egyptian Journal of Pharmaceutical Sciences (1994), 35(1-6), 91-112
CODEN: EJPSBZ; ISSN: 0301-5068
PUBLISHER: National Information and Documentation Centre
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Seven analogs of medetomidine and naphazoline were synthesized and evaluated for their .alpha.1- (aorta) and .alpha.2- (platelet) activities. The analogs were composed of 2- and 4-substituted imidazoles and imidazolines attached through a methylene bridge to either an .alpha.- or .beta.-naphthalene ring system. In general the .alpha.-naphthlene analogs were found to be the most potent inhibitors of platelet aggregation. .alpha.-Naphthalene analogs were partial agonists while the .beta.-naphthalene analogs were antagonists in .alpha.1-adrenergic system (aorta).

IT 137967-82-9P 166034-65-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and adrenergic activities of medetomidine and naphazoline analogs)

RN 137967-82-9 CAPLUS
CN 1H-Imidazole, 4-[1-(2-naphthalenyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



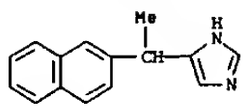
● HCl

RN 166034-65-7 CAPLUS
CN 1H-Imidazole, 4-[1-(2-naphthalenyl)ethyl]-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

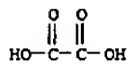
CRN 137967-88-5
CMF C15 H14 N2

L11 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2003 ACS (Continued)



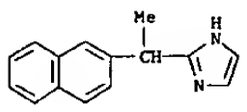
CM 2

CRN 144-62-7
CMF C2 H2 O4

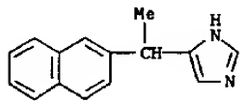


IT 137967-85-2P 137967-88-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and adrenergic activities of medetomidine and naphazoline analogs)

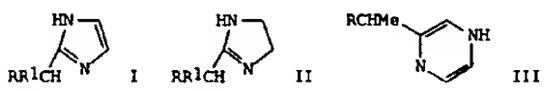
RN 137967-85-2 CAPLUS
CN 1H-Imidazole, 2-[1-(2-naphthalenyl)ethyl]- (9CI) (CA INDEX NAME)



RN 137967-88-5 CAPLUS
CN 1H-Imidazole, 4-[1-(2-naphthalenyl)ethyl]- (9CI) (CA INDEX NAME)



L11 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:106173 CAPLUS
DOCUMENT NUMBER: 116:106173
TITLE: Synthesis and .alpha.-adrenergic activities of 2- and 4-substituted imidazoline and imidazole analogs
AUTHOR(S): Amemiya, Yoshiya; Hong, Seoung S.; Venkataraman, Burrah V.; Patil, Popat N.; Shams, Gamal; Romstedt, Karl; Feller, Dennis R.; Hsu, Fu Lian; Miller, Duane D.
CORPORATE SOURCE: Coll. Pharm., Ohio State Univ., Columbus, OH, 43210, USA
SOURCE: Journal of Medicinal Chemistry (1992), 35(4), 750-5
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB Analogs I-III (R = 1-naphthyl, 2-naphthyl; R1 = H, Me) of medetomidine and naphazoline were synthesized and evaluated for their .alpha.1 (aorta) and .alpha.2 (platelet) activities. In general the 1-naphthalene analogs were the most potent inhibitors of epinephrine-induced platelet aggregation. Of considerable interest was the fact that I-III (R = 1-naphthyl) were antagonists in an .alpha.1-adrenergic system (aorta). Thus, appropriately substituted naphthalene analogs of medetomidine and naphazoline provide a spectrum of .alpha.1-agonist, .alpha.1-antagonist, and .alpha.2-antagonist activity.

IT 137967-82-9P 137967-85-2P 137967-86-3P 137967-88-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and adrenergic activity of)

RN 137967-82-9 CAPLUS
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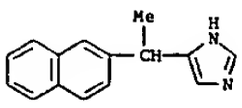

● HCl

RN 137967-85-2 CAPLUS
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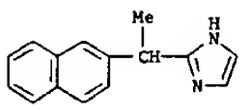
L11 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2003 ACS (Continued)



RN 137967-86-3 CAPLUS
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CRN 137967-85-2
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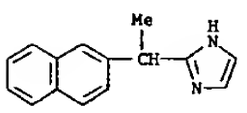

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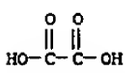

RN 137967-88-5 CAPLUS
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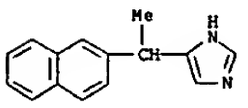
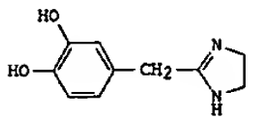
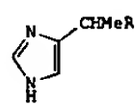


L11 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:15364 CAPLUS
DOCUMENT NUMBER: 116:15364
TITLE: Structure-activity studies of new imidazolines on adrenoceptors of rat aorta and human platelets
AUTHOR(S): Venkataraman, B. V.; Shams, G.; Hamada, A.; Amemiya, Y.; Tantishaiyakul, V.; Hsu, F.; Fashempour, J.; Romstedt, K. J.; Miller, D. D.; et al.
CORPORATE SOURCE: Coll. Pharm., Ohio State Univ., Columbus, OH, 43210, USA
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (1991), 344(4), 454-63
CODEN: NSAPCC; ISSN: 0028-1298
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



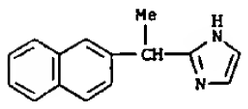
II

AB Potencies of new arom. substituted fluoro or iodo analogs of catecholimidazoline (I) on functional responses in rat aorta (.alpha.1) and platelets (.alpha.2) were quantified. When compared either on the basis of EC50 or the dissocn. const. (KA), 5-fluorocatecholimidazoline was as potent as the ref. .alpha.1-adrenoceptor agonist, phenylephrine in the vascular tissue. The max. contraction of aorta produced by the fluoro analog was, however, 17% higher than that of phenylephrine. The time required for 1/2 relaxation of the tissue after 5-fluoro hydroxy imidazoline was at least twice as long as that of the phenylephrine. The catechol moiety as well as fluorine substitution at the crit. 5-position of the arom. ring is essential for higher .alpha.1 adrenoceptor-mediated potency. As compared to the fluoro analogs, the adrenoceptor-mediated potencies of iodo-analogs were relatively weak on vascular tissue. Naphazoline and its analogs were partial agonists on vascular tissue with dissocn. consts. which ranged from 110 to 2600 nmol/L. Imidazole analogs (II, R = naphthyl or xylene), were generally less potent agonist than the imidazolines by one order of magnitude. The vascular effects of all agonists were competitively blocked by prazosin with KB values which ranged from 0.04 to 0.48 nmol/L. Since the variation in KB values were within normal limits, the action of new imidazolines on rat aorta appears to be mediated mainly by the activation of the .alpha.1-adrenoceptor. Prazosin 10 nmol/L abolished the vascular response of some partial agonists. This indicates a slightly different mode of interaction of agonists with the transduction process. Carbon 4-substituted imidazolines produced little or no .alpha.1 adrenoceptor-mediated intrinsic activity, but competitive receptor blocking potency was comparable to that of phentolamine. Medetomidine was a partial agonist on the rat aorta with a KA of 260 nmol/L. When investigated as a blocker, the KB of medetomidine against phenylephrine was approx. 5600 nmol/L. The variation in the latter value was high. In acetylsalicylic acid-treated human platelets, the .alpha.2-adrenoceptor-mediated aggregatory effect of all fluoro analogs was weak. Iodo or naphazoline analogs did not initiate platelet aggregation but blocked the aggregation induced by epinephrine. The affinity of naphazoline for the .alpha.2-adrenoceptor was 1100 nmol/L. The IC50 of medetomidine for platelet anti-aggregatory effect was 3300 nmol/L, which compares favorably with other imidazoline type of blockers of platelet aggregations. Sympathomimetic vasoconstrictor actions and platelet aggregation effects of these compds. can be dissocd. Some vasoconstrictors were antiaggregatory. The structure-activity relationships of the two receptor systems, namely rat aorta (.alpha.1) and platelets (.alpha.2), are discussed.

L11 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2003 ACS (Continued)

IT **137967-85-2 137967-88-5**
RL: BIOL (Biological study)
(.alpha.-adrenoceptors of aorta and human platelets interaction with, structure in relation to)

RN 137967-85-2 CAPLUS
CN 1H-Imidazole, 2-[1-(2-naphthalenyl)ethyl]- (9CI) (CA INDEX NAME)



RN 137967-88-5 CAPLUS
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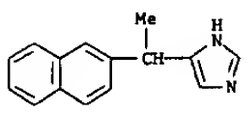

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FULL ESTIMATED COST	39.26	486.32

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
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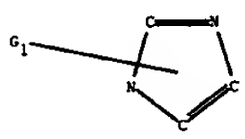

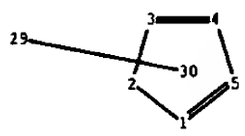

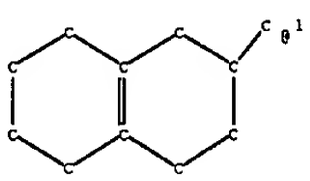

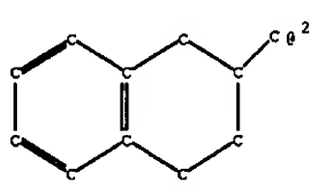

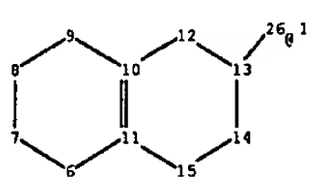

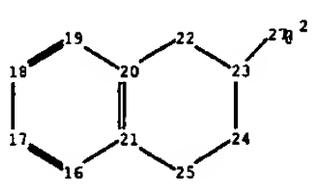

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ring bonds :
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exact/norm bonds :
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